May 23, 1950.

Mr. Carlton Fredericks, Institute of Nutrition Research, 62 West 45 Street, New Ork 19, N.Y.

Dear Mr. Fredericks,

Thank you for your reply and extended reply to my hasty query concerning the character of the evidence for your statement that "the father's diet before conception also affects the child." I must certainly agree with you that this evidence is quite diffuse when it rests on a) primitive practices b) an irrelevant issue — the <u>fertility</u> of the male as influenced by mutrition, which can scarcely be questioned — and c) unpublished and undocumented experiments.

It may help a little to go over your letter paragraph by paragraph in numerical order.

- P2. I am not sure what you mean by "Murphy's dictum". If you mean that genetic mutations can occur at all times, I agree. But then you must show that nutrition has a direct effect on mutation rates, a conclusion which few American geneticists will accept.
- P3. Our medical library has a copy of a book entitled "Nutrition and Physical Degeneration" by Neston Price, published in 1939-40 by Hoeber rather than by the American Academy of Applied Nutrition. Is this the book to which you refer? On page 342 there is a passing mention (not "details of an experiment") of a series of four litters by the same dachshund sire, in each of which there occurred pups with deformities. [There is a slight inconsistency: Fig. 120 refers to <u>five</u> bitches, but this may have been a typographical error.] There is no mention here of any evidence that the hereditary abnormalities transmitted by the propositus sire were induced by his mutritional status, nor does your letter refer to any sort of control, which might raise this observation to the status of an experiment. Price's conclusion that the genotype of the male parent may influence congenital abnormalities is not objectionable.
- P4. I would be very much interested to see the details of the experiments on cats would you favor me with a repaint when they are published? This type of experiment requires a genetic purity of parental lines that I doubt has been attained in cats.
- P5. While I agree that due consideration must be given to primitive practices in social organization and hygienic behavior, for civilised peoples have

a great deal to learn about how to live, you can hardly cite this as evidence. After all, some primitive peoples have not connected intercourse with conception, and others placate the gods of the elements, which does not imply that our biology and our meteorology are false. But even if this type of argument were acceptable, the emamples cited by Price might be directed towards the maintenance of fertility, nutritional effects on which I could not controvert.

- P.6. Agreed, or rather agreeable.
- P7, You are begging the question, not citing evidence.
- P8. This might be interesting, if there could be adequate controls. Was the mother's nutrition independent of the father's? Are you ighoring the discordant examples, of which there must be many, and selecting only those chance sequences which fit the concept? This type of reasoning should be backed up by a careful statistical analysis. Otherwise, anyone with a bread experience can selecté, consciously or otherwise, those sequences which fit his a priori concepts.
- P9. Perhaps they agree that the evidence is grossly inadequate.
- Plo. I think you have misinterpreted the Drosophila experiments. I don't know of anyone who has claimed to restore the normal gentotype by nutritional means. Some mutants may be modified in their immediate phenotypic expression by nutrition, which is a very different thing. I am certainly unacquainted with any suggestion of an influence of paternal nutrition.
- Pll. Heredity is not immutable at least with respect to apontaneous mutations, and genetic changes induced by X-rays and certain very toxic chemicals. I do not deny that the possibility exists of nutritional effects in the male, but we are not discussing this. We are discussing whether there is any evidence for it, and of this I am left entirely unconvinced. My colleagues in this department, many of whom are actively engaged both in nutritional and genetic factors in animal reproduction, are of a like mind,

This criticism is perhaps close to carping, directed as it is against a very narrow aspect of your highly commendable work. Certainly we do not wish to neglect the mutritional status of fathers, for many reasons besides the likelihood of fertility effects and the remote possibility of effects on congenital malformations. The lay public is however often poorly informed on these matters, in particular with the current Lysenkist controversy. It is important on that basis to be extremely cautious in propagating well-established facts as distinguished from speculations. For my part, I would be extremely hesitant to propound uncertain data in another specialty than my own, for example nutrition.

Sincerely yours,

Joshua Lederberg Assistant Professor of Genetics